Overview of Nuclear Medical Imaging Instrumentation and Techniques*

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Abstract. Nuclear medical imaging is a well established method for obtaining information on the status of certain organs within the human body or in animals. This paper presents an overview of two commonly used methods, namely SPECT (single photon emission computed tomography) and PET (positron emission tomography), as well as the emerging method of intra-operative probes with imaging capability. The discussion concentrates on the instrumentation requirements for these systems and on the potential for incorporating scintillating, wavelength-shifting, and fiber optic light guides into them.

INTRODUCTION

Nuclear medical imaging is a generic term that covers many imaging techniques, with the common theme being that ionizing radiation originating from within the body is detected and imaged in order to determine something about the physiology or anatomy of the subject (1-5). The ionizing radiation is often in the form of a radioisotope that is incorporated into a biologically active compound (*i.e.* a drug) that is introduced into the body (in trace quantities) either by injection or inhalation. This compound then accumulates in the patient and the pattern of its subsequent radioactive emissions is used to estimate the distribution of the radioisotope and hence of the tracer compound.

Since the image that is produced is of the distribution of a drug within the body, nuclear medical imaging is capable of targeting where certain metabolic processes occur and measuring the rate at which these processes take place. Thus, it is able to determine whether the biochemical function of an organ is impaired, while many other forms of medical imaging (such as x-ray, ultrasound, or magnetic resonance techniques) are usually confined to determining the physical structure of the organ. It is therefore most frequently used in organs and diseases where biological function is of primary importance and information on physical structure is either irrelevant or ambiguous. Examples are neurological diseases (such as Alzheimer's disease) where physical affects are only observable on a microscopic level, heart disease (where the relative vigor of the tissue is of primary importance), or oncology (cancer), where the metabolism rate gives

* This work was supported in part by the U.S. Department of Energy under Contract No. DE-AC03-76SF00098, and in part by Public Health Service Grants No. R01-CA48002, R01-CA67911, and P01-HL25840 from the National Institutes of Health.

valuable information on whether tissue is cancerous and how it responds to treatment.

While the instruments used to detect and image this radiation are often similar to those used for high energy or nuclear physics experiments, there are many important differences between the requirements for medical imaging and the requirements for detecting subatomic particle interactions. This paper describes two common nuclear medical imaging techniques, namely SPECT and PET, with emphasis on the requirements of the detection system and the reason for those requirements. Some discussion of the potential for use of various forms of optical fibers (scintillating, wavelength-shifting, and purely transmitting light guides) in these applications is given, concluding with a description of a new imaging system (an intra-operative probe) that utilizes optical fiber technology.

GENERAL CONSIDERATIONS

Imaging emissions from a radioactively labeled drug necessarily involves selecting a radioisotope, and the choice of the radioisotope used for a given nuclear medical technique involves a tradeoff of several factors. The radioisotopes most commonly used are gamma ray emitters (or positron emitters, whose net result is a pair of annihilation photons), as gamma rays can penetrate the body and be imaged with external detectors more easily than other forms of ionizing radiation. In general, high energy gammas penetrate the body easily (and so have high detection efficiency), but low energy emissions are convenient to detect in small detector volumes and are easy to shield. Most medically used isotopes have monochromatic emissions between 60 keV and 511 keV. Radioisotopes with long half lives are convenient for drug manufacture and distribution, as both the synthesis of complex biochemicals and the delivery from the place of manufacture to the patient can be time consuming. Radioisotopes with short half lives usually result in a lower radiation dose to the patient, as practical considerations limit imaging times to less than two hours and emissions that occur after the imaging session is complete contribute to patient dose but not to image quality. Most medically used isotopes have half lives between 1 minute and several days. Finally, chemistry of the radioisotope is important, as it must be incorporated into complex, biologically active compounds. Isotopes of hydrogen, carbon, oxygen, and nitrogen are most desirable, as most biochemicals contain at least one of these elements, but many other elements have been incorporated into biologically active compounds.

The detection system should be very efficient, as safety concerns cause regulatory agencies to limit the total radiation dose that can be administered to a patient. Thus, reduced statistical noise cannot be obtained by increasing the activity (*i.e.* the signal source), and so must be obtained by maximizing detection efficiency. At the gamma ray energies used for nuclear medical imaging (60–511 keV), the attenuation length in tissue is 5–10 cm. This is similar to the distance that gamma rays often need to travel to exit the body, so a significant fraction of the internally emitted gamma rays interact within the patient. Due to the low effective atomic number of tissue, most of these interactions result in Compton scatter, and most of the scattered photons continue to undergo Compton scattering until they eventually leave the body. While the net radiation flux impinging upon the detector usually contains 10%–50% unscattered gammas (which can be used to form an accurate image), the majority are Compton photons that form a background. The detection system must then be capable of reducing this Compton background, usually by measuring the energy of each detected photon with 8%–20% full-width at half-maximum (fwhm) resolution. Finally, a image cannot be

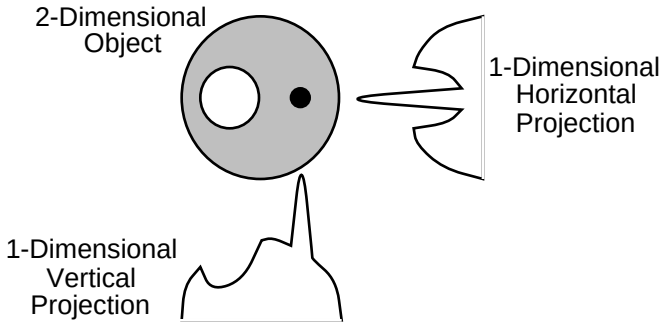

FIGURE 1. Computed Tomography. The 1-dimensional horizontal and vertical projections (the line integral of the density along parallel horizontal and vertical lines) are shown adjacent to the 2-dimensional object that they were taken of. Computed tomography is the process of reconstructing the 2-dimensional object given its 1-dimensional projections from all angles.

formed unless the direction of photon travel is known, so the detector system must be capable of determining this direction.

Both SPECT and PET make use of the mathematical technique of computed tomography to form images (4, 6, 7). Briefly stated, computed tomography is a process whereby a 2-dimensional image of an object is formed using multiple 1-dimensional projection images of that object. This is demonstrated in Figure 1. The 2-dimensional object in question is a large circle of uniform density in which a medium circle of lower density and a small circle of higher density are embedded. The one dimensional projection of the object in the vertical direction is shown below the object. This projection is what would result if a planar x-ray of the object were taken, and represents the line integral of the 2-dimensional object's density along parallel, vertical lines that cross the object. The hemisphere corresponding to the large circle is clearly seen, modified by a dip due to the low density region and a spike due to the high density region. To the right of the object is its one dimensional projection in the horizontal direction. Again the hemisphere with the associated dip and spike are seen, but the positions of the dip and spike have changed because of the change in viewing angle. What the details are beyond the scope of this paper, taking one dimensional projections at all angles around an object (not just the two shown in Figure 1) provides enough information to reproduce a 2-dimensional image of the object.

SPECT

SPECT (Single Photon Emission Computed Tomography) (7, 8) employs radioisotopes that are single gamma emitters. The most commonly used isotopes are ^{99m}Tc (141 keV), ^{201}Tl (135 keV and 167 keV), and ^{123}I (159 keV), although other isotopes with energies ranging from 80 keV to 511 keV are occasionally employed. Although SPECT radioisotopes tend to be challenging to incorporate into biologically active compounds, they have been included in drugs that show metabolic activity (such as ^{99m}Tc-Sestamibi, which concentrates in mitochondria), blood flow (such as ^{201}Tl for the heart and ^{99m}Tc-HMPAO for the brain), presence of certain forms of cancer (such as ^{67}Ga-Citrate, ^{123}I-MIBG, and ^{99m}Tc-MDP), liver function (such as ^{99m}Tc-sulphur colloid), and a variety of other imaging agents.

A typical SPECT camera is shown schematically in Figure 2. The emitted gamma rays are detected by two-dimensional position sensitive detectors. The direction of the

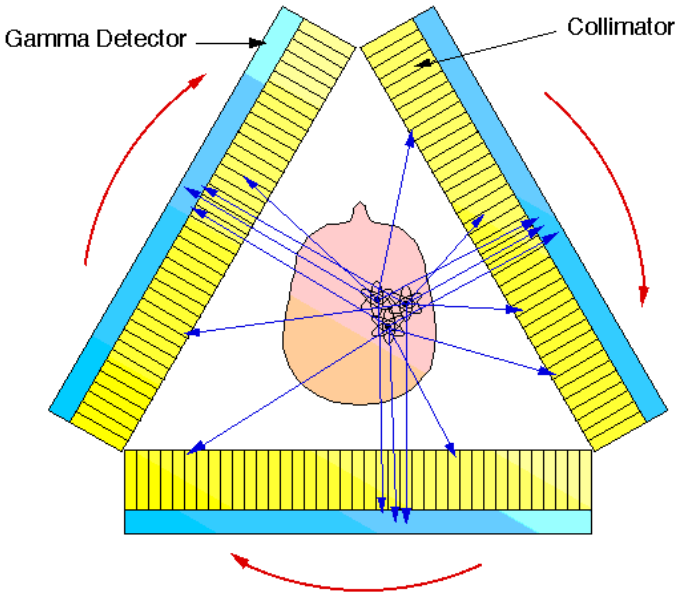

FIGURE 2. SPECT Camera Schematic. A collimator blocks gamma rays that are not traveling normal to its surface, and those gammas that pass through the collimator are detected with a planar position sensitive detector. The assembly rotates around the patient to provide the many projections necessary for computed tomography.

gamma rays is determined by a collimator placed between the detector array and the patient — photons that are not traveling in the desired direction are absorbed by the collimator. The collimator and detector combination (and their associated electronics and mechanical support) form what is known as a gamma camera "head". While multiple heads increase the detection efficiency of a SPECT camera (and the cost), there is little efficiency gain above three heads, so most SPECT cameras have between one and three heads. Each head measures a planar projection of the activity in the patient, and by simultaneously rotating the heads, the requisite set of projections to perform computed tomography is obtained.

The most commonly used gamma detector for SPECT is the Anger camera, which is named for its inventor (9). A schematic of an Anger camera is shown in Figure 3. A

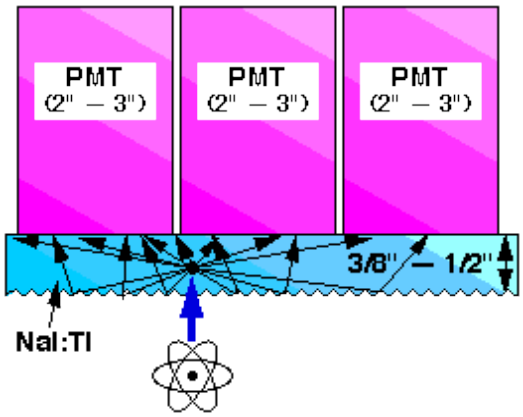

FIGURE 3. Anger Camera. Scintillation light from gamma ray interactions is detected by multiple photomultiplier tubes. The interaction position is determined by the ratio of the analog signals, and the energy by the analog sum of the signals.

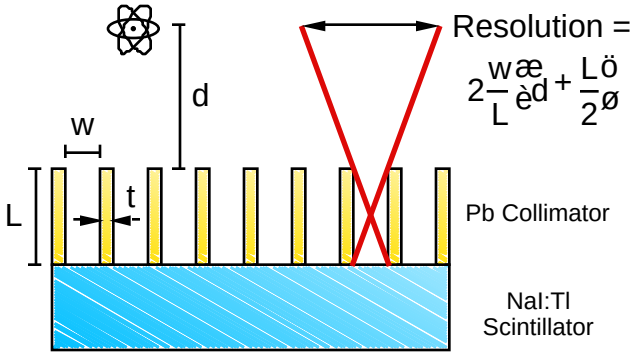

FIGURE 4. Collimator Cross Section. The spatial resolution and efficiency of SPECT are determined by the collimator.

plate of NaI:Tl scintillator crystal is optically coupled to many photomultiplier tubes. When a gamma ray interacts in the crystal, the resulting scintillation photons are emitted isotropically and are detected by several of the photomultiplier tubes. The position of the gamma ray interaction is then determined by the analog ratio of the photomultiplier tube output signals, and the gamma ray energy is determined by the sum of these signals.

The thickness of the NaI:Tl crystal determines the efficiency of the camera. As its attenuation length for 140 keV gamma rays is 4 mm, the 9–12 mm thick plates commonly employed in SPECT systems provide nearly complete absorption. The scintillator surface not coupled to the photomultiplier tubes strongly affects the light distribution observed by the photomultiplier tubes and is often prepared with a proprietary surface treatment to optimize both position and energy resolution. Special care is needed near the edges of the scintillator crystal, as reflections from the side of the crystal cause the dependence of the measured light distribution on the interaction position to be much weaker near the sides than near the middle. A typical Anger camera has 9% fwhm energy resolution and 3.5 mm fwhm position resolution for 140 keV gammas.

While the Anger camera is an important component of a SPECT imager, the performance of a SPECT camera is almost entirely determined by the collimator (10). Figure 4 shows a schematic drawing of a parallel hole collimator. The collimator is usually made from cast lead with hexagonal cross section holes arranged in a honeycomb fashion. Each hole can be thought of as having a diameter w and a length L, separated from its neighbors by a lead septum of thickness t (typically 0.2 mm). The spatial resolution is determined by the collimator geometry and is given by

$$\text{Resolution} = 2\frac{w}{L}\left(d + \frac{L}{2}\right), \qquad (1)$$

where d is the distance from the collimator surface to the object being imaged. From Equation 1 we can see that the resolution scales linearly with the aspect ratio w/L of the collimator, and as L is typically 1–3 cm and d is typically tens of centimeters, increases roughly linearly with the distance d from the collimator. While arbitrarily high spatial resolution can be achieved with a collimator by reducing w/L, more modest spatial resolution is usually obtained because this aspect ratio greatly affects the efficiency. The fraction of gammas that are transmitted through the collimator is

$$\text{Efficiency} = \left(\frac{w}{2L}\right)^2, \qquad (2)$$

so while the resolution improves linearly with w/L, the efficiency decreases quadratically. For a typical “all-purpose” collimator, the spatial resolution is 6.2 mm

fwhm at a distance of 5 cm and the efficiency is 0.023%. From this we see that the spatial resolution of a SPECT image is not determined by the resolution of the Anger camera (which is known as the intrinsic resolution), but by the collimator.

Based on current SPECT cameras, the gamma ray detector requirements for SPECT are, in order of decreasing importance, (1) >85% detection efficiency (to minimize statistical fluctuations), (2) <15 keV fwhm energy resolution (to reject Compton scatter events), (3) <3.5 mm fwhm intrinsic position resolution (to avoid degrading the collimator resolution), (4) <\$15/cm^2 parts cost (SPECT cameras are widely available commercially), and (5) <2000 μs cm^2 dead time product (single event dead time multiplied by detector area affected — low collimator efficiency implies low counting rates).

PET

PET (Positron Emission Tomography) (11) employs radioisotopes that are positron emitters. The most commonly used isotopes are ^{18}F, ^{11}C, ^{15}O, and ^{13}N, although other isotopes are occasionally employed. A great number of biologically active compounds have been synthesized with these isotopes, they have been included in drugs that show metabolic activity (such as ^{18}F-FDG, a sugar analog), blood flow (such as ^{15}O-water), a variety of neurotransmitters (such as ^{18}F-Dopamine), and a large variety of other imaging agents (12).

A typical PET camera, shown schematically in Figure 5, consists of a planar ring of small photon detectors, with each photon detector placed in time coincidence with *each* of the individual photon detectors on the other side of the ring. When a pair of photon detectors simultaneously detect 511 keV photons, a positron annihilated somewhere on the line connecting the two detectors. The method of using time coincidence between two detectors (rather than a collimator and one detector) to restrict events to a line is known as electronic collimation, and is much more efficient than the mechanical collimation used in SPECT. The set of all lines connecting detectors (known as chords) makes the requisite set of projections to perform computed tomography for a single plane. Multiple detector rings are stacked on top of each other to obtain images from multiple slices, and thus a three-dimensional image of the patient. Planes of tungsten

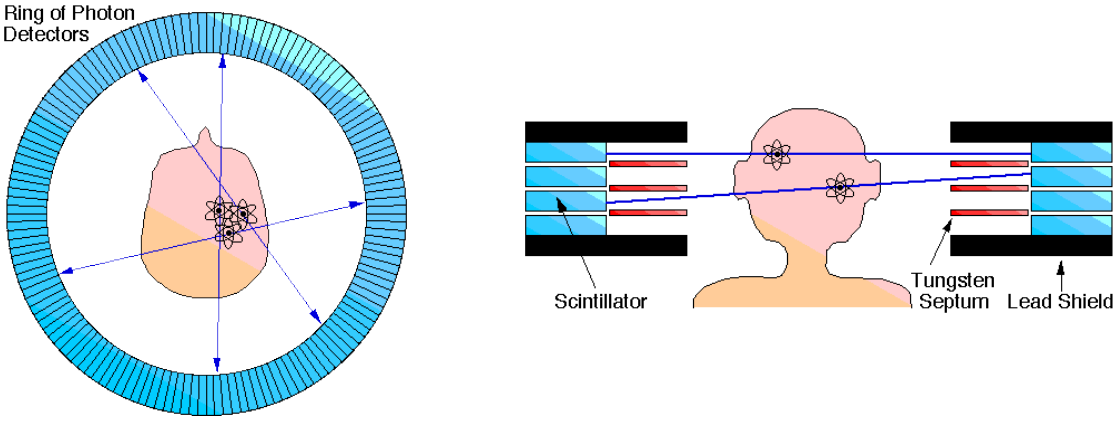

FIGURE 5. PET Camera Schematic. Positron annihilations yield back to back 511 keV photons, which are individually detected in a ring of photon detectors, shown on the left. Pairs are identified by time coincidence. Multiple rings are stacked up, as shown on the right, to create a 3-dimensional image.

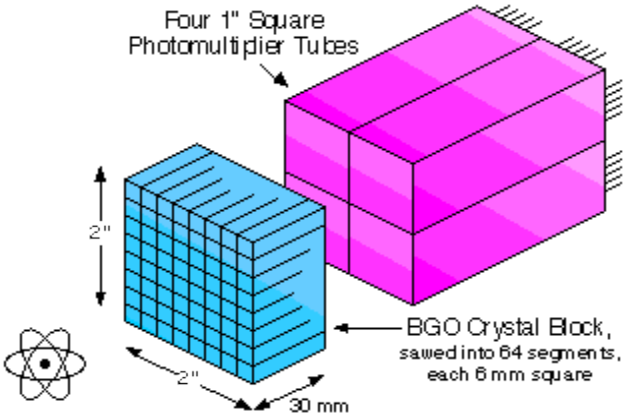

FIGURE 6. PET Detector Module. Scintillation light from gamma ray interactions is detected by multiple photomultiplier tubes. The interaction position is determined by the ratio of the analog signals, and the energy by the analog sum of the signals.

septa placed between detector planes are often used to shield the detectors from Compton scattered photons emanating from other parts of the body, and images taken in this geometry are often known as "2-D PET" images. Coincidences between nearly adjacent "cross-plane" rings are usually added to the closest "direct plane" to increase detection efficiency. If the septa are removed, the efficiency is greatly increased (as coincidences from widely separated planes can be accepted), but the backgrounds also increase significantly. However, the signal to noise ratio improves in some situations, and this mode of operation is known as "3-D PET."

The most commonly used PET detector module is known as a block detector, and a schematic is shown in Figure 3 (13). A block of BGO scintillator crystal is partially sawn through to make a group of quasi-independent crystals that are optically coupled to four photomultiplier tubes. When a gamma ray interacts in the crystal, the resulting scintillation photons are emitted isotropically but the saw cuts limit (but does not entirely prevent) their lateral dispersion as they travel toward the photomultiplier tubes. The position of the gamma ray interaction is then determined by the analog ratio of the photomultiplier tube output signals, and the gamma ray energy is determined and a timing pulse generated by the sum of these signals.

The thickness of the BGO crystal determines the efficiency of the camera. As its attenuation length for 511 keV gamma rays is 1.2 cm, the 30 mm thick BGO crystals commonly employed in PET systems provide nearly complete absorption. The coincidence timing efficiency is limited by the decay time of BGO — the photoelectron (p.e.) rate immediately after a 511 keV photon interaction is approximately 0.5 p.e./ns. A typical PET detector module has 20% fwhm energy resolution, 2 ns fwhm timing resolution and 5 mm fwhm position resolution for 511 keV gammas.

Based on current PET cameras, the gamma ray detector requirements for PET are, in order of decreasing importance, (1) >85% detection efficiency (to minimize statistical fluctuations), (2) <5 mm fwhm position resolution (to obtain good spatial resolution), (3) <\$100/cm^2 parts cost (PET cameras are widely available commercially), (4) <1 μs cm^2 dead time product (single event dead time times detector area affected — high counting rates are often encountered), (5) <2 ns timing resolution (to identify coincident pairs), and (6) <100 keV fwhm energy resolution (to reject Compton scatter events) (14).

OPTICAL FIBER USE IN NUCLEAR MEDICAL IMAGING

The potential for use of optical fibers (including scintillating fibers, wavelength-shifting fibers, and fiber optic light guides) in nuclear medical imaging equipment is somewhat limited by the low energies of the radiation that must be detected and imaged. Most geometries that utilize optical fibers end up delivering less than 10% of the light impinging on one end of the fiber to the opposite end of the fiber, even when using high quality, double clad fibers. This reduction in efficiency would often degrade the signal to the point where the statistical noise becomes too large to measure the gamma ray energy with sufficient resolution.

As an example, let us consider SPECT, in which 140 keV gammas must be imaged with ≤10% fwhm energy resolution. If statistical noise was the only effect that contributed to energy resolution degradation, this would imply that ≥550 quanta must be detected. If NaI:Tl scintillator is used (one of the most luminous scintillators known), its 38,000 photon/MeV conversion efficiency implies that ~5,300 scintillation photons will be produced by a 140 keV interaction. If a photomultiplier tube with 20% quantum efficiency is used to detect these photons, approximately 1000 photoelectrons will be detected *provided* that the coupling between the scintillator and photomultiplier tube is 100% efficient. Obviously, the <10% coupling efficiency afforded by optical fibers will yield too small a signal to meet the energy resolution requirement.

Optical & Wavelength-Shifting Fiber Use in PET

However, there are several proposals for nuclear medical imaging equipment that incorporate optical fibers. The first is a PET detector that uses quartz fibers to couple individual LSO scintillator crystals with 2 mm square cross section to a position sensitive photomultiplier tube (15). These crystals must be packed together into a circular, gap-free array around the patient (in this case, a small animal), and the significant dead area at the perimeter of the position sensitive photomultiplier tube does not allow them to be directly coupled to the crystals. Therefore, 2 mm diameter, 24 cm long, double clad quartz fibers are used to couple the scintillator crystals to the photosensors. This arrangement, shown in Figure 7, moves the photomultiplier tubes to a larger radius to allow the scintillators to be packed without gaps.

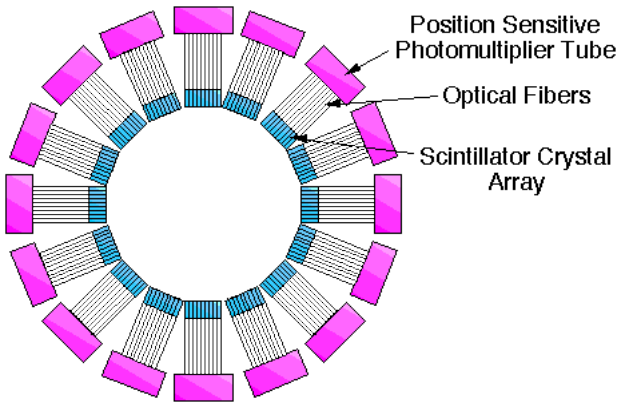

FIGURE 7. PET Camera Utilizing Optical Fibers. Scintillator crystal arrays are coupled to position sensitive photomultiplier tubes with arrays of optical fibers. This allows the scintillators to be close packed even though the photomultiplier tubes have significant dead area.

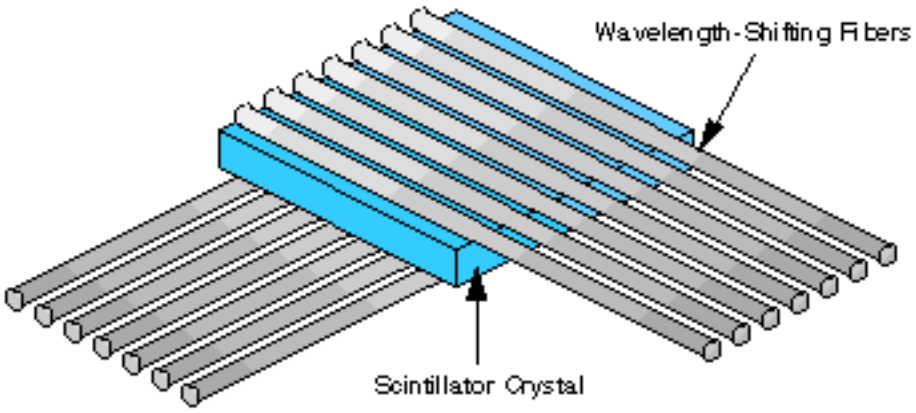

FIGURE 8. PET Camera Utilizing Wavelength-Shifting Fibers. Scintillation emissions from a thin plate of scintillator crystal are absorbed by orthogonal arrays of wavelength-shifting fibers. These fibers re-emit photons of a lower energy, with the interaction position determined by coupling the fiber arrays to position dependent photomultiplier tubes that identify the fibers that emit photons. Several layers are stacked on top of each other, and additional photosensors are required to measure energy and timing.

Other proposed PET detector modules utilize wavelength-shifting fibers coupled to thin plates of LSO scintillator crystal (16, 17). Arrays of fibers are placed in orthogonal orientations on either side of the plate, and since the plate is only a few millimeters thick, the spread of scintillation light in the crystal is small and the majority of the signal is collected in a single wavelength-shifting fiber. The fiber absorbs this primary scintillation light and re-emits lower energy photons, some of which are transported down the length of the fiber. A position-sensitive photodetector is coupled to each array of fibers and determines the position of interaction based on which fibers signals are observed in. Multiple scintillator / fiber layers are stacked on top of each other in order to achieve the requisite gamma interaction fraction. Additional photosensors are employed to measure the total energy of the gamma and produce a timing signal, as the signal transmitted by the fibers is only tens of electrons, which is insufficient for sufficiently accurate timing or energy measurement.

Optical & Scintillating Fiber Use in Intra-Operative Probes

Finally, a combination of scintillating and transparent optical fibers have been proposed for use with an intra-operative probe system (18). When surgically removing cancerous tumors, it is desirable to remove all cancer cells associated with the tumor. Often extra, non-cancerous tissue around the tumor is removed in order to ensure this. However, removal of additional tissue can have serious side-effects in some organs, such as the brain. One method for maximizing tumor / normal tissue removal is to inject the patient (before surgery) with a positron emitting drug that accumulates in tumors (such as ^{18}F-FDG). After the bulk of the tumor has been removed, a positron-sensitive probe is inserted into the surgical opening and placed next to the suspect tissue to determine whether it has high radiotracer concentration (*i.e.* is cancerous) and so should also be removed. A positron-sensitive (rather than gamma-sensitive) imager is used because there is little room in the incision, so the large detector volumes necessary for efficient 511 keV photon detection and for shielding the detector from the tremendous flux of annihilation photons from the rest of the body are not practical. Because of the short range of positrons in tissue (~0.5 mm), a detector placed in contact with the tissue

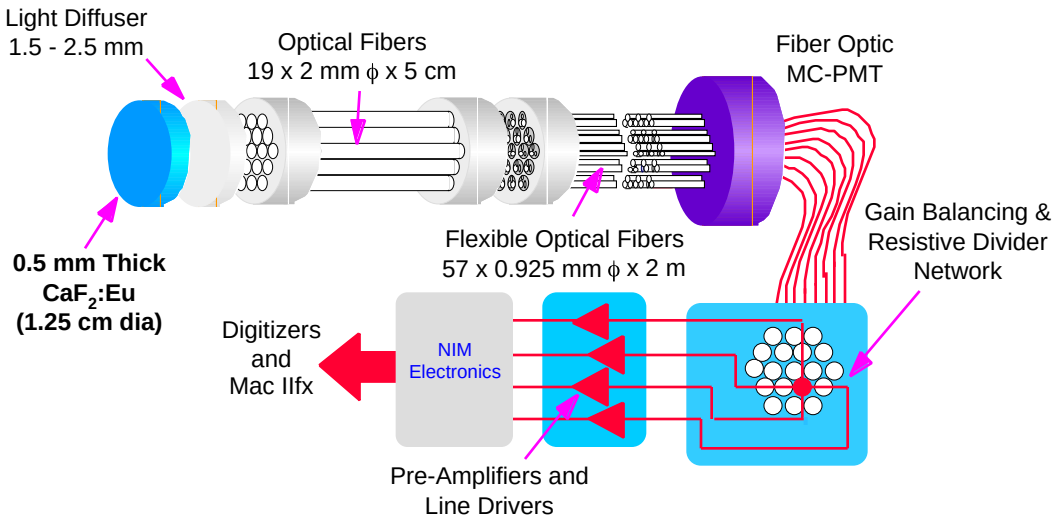

FIGURE 9. Intra-Operative Probe. A thin CaF_2:Eu scintillator crystal detects positrons from tissue that has been injected with a tumor-avid, positron-emitting drug. The resulting scintillation light is coupled using optical fibers to a position-sensitive photomultiplier tube, and Anger logic used to determine the interaction position. A bundle of BGO scintillator fibers placed between the light diffuser and the transparent optical fibers can be used to reject 511 keV photon interactions in the CaF_2:Eu.

form a "contact" image the underlying positron distribution — computed tomography is not used.

The schematic of such a detector is shown in Figure 9. The scintillator chosen is a thin plate of CaF_2:Eu because its relatively low density and atomic number make it relatively insensitive to gamma rays, while its high light output (19,000 photons/MeV) provides a relatively high signal. An array of optical fibers carries the scintillation light to a position sensitive photomultiplier tube, and the position of the interaction determined by Anger logic (*i.e.* the analog ratio of signals observed in the position sensitive photomultiplier tube). While this system is effective, there is still significant background due to annihilation photon interaction in the CaF_2:Eu. In order to reduce this background, the first centimeters of optical fiber are replaced with optical fibers made of BGO scintillator. This scintillator is highly efficient at detecting annihilation photons, and the difference in scintillation decay times (300 ns for BGO, 1 μs for CaF_2:Eu) allows the use of a "phoswich" technique, in which a single photomultiplier tube can separate signals in the two scintillator crystals based on their decay time. When the signal from the CaF_2:Eu (assumed to be from a positron interaction) is required to be in time coincidence with ~511 keV energy deposit in the BGO scintillator (assumed to be from an annihilation photon from the same positron interaction), the image contrast improves significantly.

CONCLUSION

Nuclear techniques have been used for over 50 years to image biochemical processes in living organisms. Most involve imaging photons with energies of 100–511 keV, as these photons can be produced by radioisotope decay, penetrate the body with reasonable probability, and be detected with high efficiency and good spatial resolution. Detectors for these applications have seen many years of development and refinement,

and generally involved high detection efficiency (to maximize image quality for a given patient dose), good energy resolution (to minimize background from Compton scatter in the patient), low cost (as there is a competitive commercial market for these devices), and moderate (3–5 mm) spatial resolution. While optical fibers (scintillating fibers, wavelength-shifting fibers, and fiber optic light guides) are rarely used in nuclear medical imaging equipment due to their relatively low (<10%) scintillation light collection efficiency, they are used in some detector designs where other considerations (typically packaging concerns) outweigh the desire for high light collection efficiency.

ACKNOWLEDGMENTS

I would like to acknowledge Dr. Stephen Derenzo, Dr. Thomas Budinger, and Dr. Ronald Huesman for many interesting conversations, and Dr. Martin Tornai for his insights into intra-operative probes. I would like to thank Dr. Randall Ruchti and Dr. Mitchell Wayne for the opportunity to consider the impact of optical fibers on nuclear medical imaging. This work was supported in part by the Director, Office of Energy Research, Office of Biological and Environmental Research, Medical Applications and Biophysical Research Division of the U.S. Department of Energy under contract No. DE-AC03-76SF00098 and in part by the National Institutes of Health, National Cancer Institute under grants No. R01-CA48002 and R01-CA67911, and National Institutes of Health, National Heart, Lung, and Blood Institute under grant No. P01-HL25840.

REFERENCES

1. Sandler, M. P., Coleman, R. E., Wackers, F. J. T., et al., *Diagnostic Nuclear Medicine*, Baltimore, MD: Williams & Wilkins, 1996, 1549 pp.
2. Hendee, W. R. and Ritenour, R., *Medical Imaging Physics*, St. Louis, MO: Mosby Year Book, 1992, 781 pp.
3. Krestel, E., *Imaging Systems for Medical Diagnosis*, Berlin: Siemens Aktiengesellschaft, 1990, 636 pp.
4. Macovski, A., *Medical Imaging Systems*, Englewood Cliffs, NJ: Prentice Hall, 1983, 256 pp.
5. Webb, S., *The Physics of Medical Imaging*, Bristol: Institute of Physics Publishing, 1993, 633 pp.
6. Cormack, A. M. *J. Appl. Phys.* 34, 2722–2727 (1963).
7. Kuhl, D. E. and Edwards, R. Q. *Radiology* 80, 653–662 (1963).
8. Budinger, T. F., *Single Photon Emission Computed Tomography*, In Diagnostic Nuclear Medicine, (Edited by Sandler, M. P., Coleman, R. E., Wackers, F. J. T., Patton, J. A., Gottschalk, A. and Hoffer, P. B.), Baltimore, MD: Williams & Wilkins, 1996, pp. 121–138.
9. Anger, H. O. *Rev. Sci. Instr.* 29, 27–33 (1958).
10. Tsui, B. M. W., Gunter, D. L., Beck, R. N., et al., *Physics of Collimator Design*, In Diagnostic Nuclear Medicine, (Edited by Sandler, M. P., Coleman, R. E., Wackers, F. J. T., Patton, J. A., Gottschalk, A. and Hoffer, P. B.), Baltimore, MD: Williams & Wilkins, 1996, pp. 67–79.
11. Cherry, S. R. and Phelps, M. E., *Positron Emission Tomography: Methods and Instrumentation*, In Diagnostic Nuclear Medicine, (Edited by Sandler, M. P., Coleman, R. E., Wackers, F. J. T., Patton, J. A., Gottschalk, A. and Hoffer, P. B.), Baltimore, MD: Williams & Wilkins, 1996, pp. 139–159.
12. *J. Nucl. Med.* 32, 561–748 (1991).

13. Cherry, S. R., Tornai, M. P., Levin, C. S., et al. *IEEE Trans. Nucl. Sci.* NS-42, 1064–1068 (1995).
14. Moses, W. W., Derenzo, S. E. and Budinger, T. F. *Nucl. Instr. Meth.* A-353, 189–194 (1994).
15. Cherry, S. R., Shao, Y., Silverman, R. W., et al. *IEEE Trans. Nucl. Sci.* 44, 1161–1166 (1997).
16. Worstell, W., Johnson, O. and Zawarzin, V., "Development of a high-resolution PET detector using LSO and wavelength-shifting fibers," in *Proceedings of The 1995 IEEE Nuclear Science Symposium and Medical Imaging Conference* (Edited by Moonier, P. A.), San Francisco, pp. 1756-1760, 1995.
17. Williams, M. B., Sealock, R. M., Majewski, S., et al. *IEEE Trans. Nucl. Sci.* 45, 195–205 (1998).
18. Levin, C. S., Tornai, M. P., MacDonald, L. R., et al. *IEEE Trans. Nucl. Sci.* 44, 1120–1126 (1997).